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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/049,464	06/18/2002	Thomas Huenig	ALBRE 23	3876
23599	7590	03/22/2005	EXAMINER	
MILLEN, WHITE, ZELANO & BRANIGAN, P.C. 2200 CLARENDON BLVD. SUITE 1400 ARLINGTON, VA 22201			OUSPENSKI, ILIA I	
		ART UNIT	PAPER NUMBER	1644

DATE MAILED: 03/22/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/049,464	HUENIG, THOMAS	
	Examiner	Art Unit	
	ILIA OUSPENSKI	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) Responsive to communication(s) filed on 06 January 2005.
 2a) This action is FINAL. 2b) This action is non-final.
 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) Claim(s) 1-18 is/are pending in the application.
 4a) Of the above claim(s) 1-11 and 16-18 is/are withdrawn from consideration.
 5) Claim(s) _____ is/are allowed.
 6) Claim(s) 12-15 is/are rejected.
 7) Claim(s) _____ is/are objected to.
 8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) The specification is objected to by the Examiner.
 10) The drawing(s) filed on _____ is/are: a) accepted or b) objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 a) All b) Some * c) None of:
 1. Certified copies of the priority documents have been received.
 2. Certified copies of the priority documents have been received in Application No. _____.
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>9/3/2002</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. Applicant's amendment, filed 01/06/2005, is acknowledged.

Claims 1 – 18 are pending.

Claims 1 – 5 and 16 – 18 have been withdrawn from consideration by the examiner as drawn to non-statutory subject matter.

2. Applicant's election with traverse of Group II (claims 12 – 15, drawn to a method for treating virus infections with a composition containing an anti-CD28 antibody and one or two reverse transcriptase inhibitors and one or two protease inhibitors) in the reply filed on 01/06/2005 is acknowledged. Applicant further elects the species of AZT as the reverse transcriptase inhibitor and the species of RTV as the protease inhibitor.

The traversal is on the ground(s) that allegedly there is no undue burden to search inventions of Groups I and II together, as they comprise overlapping subject matter.

This is not found persuasive because the present restriction requirement is set forth under 35 USC 121 and 372, wherein the restriction criteria are based on the lack of unity of invention and not on the search burden.

The requirement is still deemed proper and is therefore made FINAL.

Claims 6 – 11 (non-elected Groups I) are withdrawn from further consideration by the Examiner, under 37 C.F.R. § 1.142(b), as being drawn to nonelected inventions.

Claims 12 – 15 are under consideration in the instant application.

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3. Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.
4. Applicant's IDS, filed 09/03/2002, is acknowledged, and has been considered.

Applicant states that the references listed on the IDS have been provided. However, reference No. 9 has not been located in the file of the instant application, and has been lined through. Applicant is invited to resubmit this reference to complete the record. The Examiner apologizes for the inconvenience to Applicant.

Reference No. 4 is a document not in the English language, and translation has not been provided. The reference has been lined through. Applicant is invited to submit an English translation of this document if he wishes this document to be considered.

5. The listing of references in the Search Report is not considered to be an information disclosure statement (IDS) complying with 37 CFR 1.98. 37 CFR 1.98(a)(2) requires a legible copy of: (1) each foreign patent; (2) each publication or that portion which caused it to be listed; (3) for each cited pending U.S. application, the application specification including claims, and any drawing of the application, or that portion of the application which caused it to be listed including any claims directed to that portion, unless the cited pending U.S. application is stored in the Image File Wrapper system; and (4) all other information, or that portion which caused it to be listed. In addition, each IDS must include a list of all patents, publications, applications, or other information submitted for consideration by the Office (see 37 CFR 1.98(a)(1) and (b)), and MPEP § 609 subsection III. A(1) states, "the list ... must be submitted on a separate paper." Therefore, the references cited in the Search Report have not been considered. Applicant is advised that the date of submission of any item of information or any missing element(s) will be the date of submission for purposes of determining compliance with the requirements based on the time of filing the IDS, including all "statement" requirements of 37 CFR 1.97(e). See MPEP § 609 subsection III. C(1).

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In particular, the reference "T. Hunig, 1998" has not been considered, because the reference has not been listed on an IDS, and a copy of this reference has not been provided.

6. The disclosure is objected to because of the following informalities: Brief Description of Drawings has not been provided.

Appropriate correction is required. See MPEP 608.01(f).

7. Claim 12 is objected to because of the following informalities: in the recitation of "well tolerated for human beings," it appears that "by human beings" has been intended. Appropriate correction or clarification is required.

8. The following is a quotation of the second paragraph of 35 U.S.C. 112.

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 12 – 15 are rejected under **35 U.S.C. 112, second paragraph**, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 12 is indefinite in the recitation of "an analogue thereto," because it is unclear whether the phrase refers back to monoclonal antibodies, CD28, or antigen receptor. Furthermore, the singular form of "analog" is inconsistent with the plural of "antibodies." A skilled artisan is not reasonably apprised of the metes and bounds of

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the claimed invention. For examination purposes, it is assumed that the recitation refers to monoclonal antibodies.

Claim 15 is indefinite in the recitation of "the drug component d) is provided in a conclusive manner," because the meaning of the recitation is unknown. A skilled artisan is not reasonably apprised of the metes and bounds of the claimed invention.

Applicant is reminded that any amendment must point to a basis in the specification so as not to add new matter. See MPEP 714.02 and 2163.06.

10. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

11. Claims 12 – 15 are rejected under **35 U.S.C. 112, first paragraph**, because the specification, while being enabling for activating monoclonal antibodies to CD28, does not reasonably provide enablement for the genus of monoclonal antibodies or and analogue thereto. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The specification does not provide a sufficient enabling description of the claimed invention.

The specification discloses only a single specificity of monoclonal antibodies, which is to CD28, while the instant claims encompass in their breadth any monoclonal antibody. Further, the specification defines analogues as substances "fulfilling the

functions described in this invention," and discloses that these can be proteins or RNA or DNA molecules with "CD28 specificity with a stimulating effect."

A person of skill in the art is not enabled to make and use any monoclonal antibody or an analogue thereof commensurate with the scope of the claims as presently recited, because it was well known in the art at the time the invention was made that molecules having highly diverse structural and biochemical properties can have "stimulating effect." Huang (Pharmacology and Therapeutics, 2000, 86: 201 – 215; see entire document) reviews e.g. on page 202 the daunting task faced by the skilled artisan in developing small molecule regulators of protein function, and notes that the process requires long periods of trial and error testing. The structure of such molecules cannot be readily envisioned by one of skill in the art based upon the guidance provided in the specification as-filed. Therefore, Applicant does not provide a sufficiently enabling disclosure regarding how to make and use monoclonal antibodies or analogues thereof which would function in the instant claimed invention, other than activating monoclonal antibodies to CD28.

Reasonable correlation must exist between the scope of the claims and scope of enablement set forth. Without sufficient guidance, the structural features of "monoclonal antibodies or analogues thereof" are unpredictable; thus the experimentation left to those skilled in the art, is unnecessarily, and improperly, extensive and undue.

The scope of the claims must bear a reasonable correlation with the scope of enablement. See In re Fisher, 166 USPQ 18 24 (CCPA 1970). "It is not sufficient to define the recombinant molecule by its principal biological activity, e.g. having protein A activity, because an alleged conception having no more specificity than that is simply a wish to know the identity of any material with that biological property." Colbert v. Lofdahl, 21 USPQ2d, 1068, 1071 (BPAI 1992).

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12. Claims 12 – 15 are rejected under **35 U.S.C. 112, first paragraph**, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The following *Written Description* rejection is set forth herein.

Applicant is not in possession of “monoclonal antibodies ... or an analogue thereto.”

The specification discloses on page 10, first full paragraph, that “analogues” can be synthetic proteins, or RNA or DNA molecules, as long as they fulfill the functions described in the invention. Applicant has discloses and reduced to practice only a single type of such “analogue,’ i.e. the antibody itself, which does not share any structural characteristics with the other disclosed types of “analogues.”

Huang (Pharmacology and Therapeutics, 2000, 86: 201 – 215; see entire document) reviews e.g. on page 202 the daunting task faced by the skilled artisan in developing specific regulators of protein function, and notes that the process requires long periods of trial and error testing. The structure of such molecules cannot be readily envisioned by one of skill in the art based upon the written description provided in the specification as-filed. Therefore, the specification does not convey to a person of skill in the art that Applicant, at the time the invention was made, had possession of the claimed “analogues.”

The Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, §1 "Written Description" Requirement make clear that if a claimed genus does not show actual reduction to practice for a representative number of species; then the Requirement may be alternatively met by reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and or chemical properties, by functional characteristics coupled with a known or disclosed correlation

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between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the genus (Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001, see especially page 1106 column 3).

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the written description inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.). Consequently, Applicant was not in possession of the instant claimed invention. See University of California v. Eli Lilly and Co. 43 USPQ2d 1398.

Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

13. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

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(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

14. Claims 12 and 15 are rejected under **35 U.S.C. 102(b)** as being anticipated by Chang et al. (US Patent 5,834,599; see entire document).

Chang et al. teach a method of treating HIV-1 infection by administering a monoclonal antibody to gp120 protein (see entire document, in particular, e.g. Summary of Invention at columns 3 – 4). Chung et al. further teach that the antibody can be administered with other agents, such as azidothymidine (AZT) or ribavirin (e.g. column 10 second paragraph).

The instant claim 12 is directed to a method of treating a retroviral infection with a monoclonal antibody preferably specific for CD28, i.e. specificity for CD28 is not required by the claim language.

Therefore the reference teachings anticipate the instant claimed invention.

15. Claims 12 and 15 are rejected under **35 U.S.C. 102(e)** as being anticipated by June et al. (US Patent 6,534,055; see entire document).

June et al. teach a method of treating HIV infection by administering anti-CD28 antibodies, together with anti-CD3 antibodies and other agents, such as anti-retroviral agents (see entire document, in particular, e.g. column 31 lines 61 – 65 and lines 30 – 33). June et al. exemplify AZT as one of anti-retroviral drugs (e.g. column 53 lines 35 – 41).

Therefore the reference teachings anticipate the instant claimed invention.

16. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

17. Claims 12 – 14 are rejected under **35 U.S.C. 103(a)** as being unpatentable over June et al. (US Patent 6,534,055; see entire document) in view of Hengge et al. (of record: reference No. 7 on IDS; see entire document).

June et al. have been discussed supra, and teach a method of treating HIV infection by administering anti-CD28 antibodies, together with anti-CD3 antibodies and other agents, such as anti-retroviral agents, e.g. AZT (see entire document, in particular, e.g. column 31 lines 61 – 65 and lines 30 – 33, and column 53 lines 35 – 41).

June et al. do not teach administering antiviral drugs according to HAART therapy, or administering them continuously.

Hengge et al. teach that HAART regimen is the current standard therapy for HIV-1 infection, and is administered continuously (see entire document, in particular, e.g. first paragraph of Introduction). Hengge et al. also teach that it is desirable to augment the remaining cell-mediated immunity in HIV patients (e.g. Introduction second

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paragraph), and that such augmentation by administering IL-2 leads to sustained immunological improvements in the majority of patients (e.g. Abstract, last paragraph).

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to apply the teaching of Hengge et al. to those of June et al. to obtain a claimed method. One of ordinary skill in the art at the time the invention was made would have been motivated to do so, because of the desirability to augment the remaining cell-mediated immunity in HIV patients, as taught by Hengge et al. From the combined teaching of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention.

It is noted that with regard to the limitation of claim 14, wherein "the drug component a) is administered once or several times in time intervals with breaks," any administration regimen would meet this limitation.

Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

18. Conclusion: No claim is allowed.

19. Any inquiry concerning this communication or earlier communications from the examiner should be directed to ILIA OUSPENSKI whose telephone number is 571-272-2920. The examiner can normally be reached on Monday-Friday 9 - 5.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 571-272-0841. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

ILIA OUSPENSKI

Patent Examiner

Art Unit 1644

March 3, 2005

Phillip Gambel
PHILLIP GAMBEL, PH.D
PRIMARY EXAMINER

Rec'd Counter 1600

3/17/05